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20. A method for treating a cancer, comprising administering to a patient in need thereof a selective endothelin B receptor antagonist compound selected from the group consisting of BQ788, IRL-1038, RES-701-1, PD-142893, and H-3596.

REMARKS

Claims 1-5 and 14-20 are presently pending. Claim 4 has been amended to more particularly point out and distinctly claim the invention; and to place the claims in condition for allowance. Support for the claim amendment can be found throughout the specification. New claims 16-20 have been added and are fully supported by the instant specification. In particular, support for claim 16 can be found, for example, on page 49, lines 10-14 of the instant specification. Support for claim 17 can be found, for example, on page 49, lines 16-18 of the instant specification. Support for claim 18 can be found, for example, on page 50, line 18 to page 51, line 3 of the instant specification. Support for claim 19 can be found, for example, on page 47, line 25 to page 48, line 22. Support for claims 20 can be found, for example, on page 16, lines 8-13 of the instant specification. Thus, no new matter has been introduced. Entry of the foregoing amendments are respectfully requested.

A marked up version of the amended claims showing the amendments is attached hereto as Appendix A. Matter that has been deleted is indicated by brackets and matter that has been added is indicated by underlining. A copy of the claims as pending after entry of the foregoing amendment is attached as Appendix B.

The Rejections Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

Claims 1-5, 14, and 15 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This rejection is in error and should be withdrawn.

The Examiner contends that Applicants were not in possession of all selective ETB antagonists at the time the application was filed. Applicants respectfully disagree with the Examiner's position that the scope of the claims is not commensurate with the specification. The Examiner appears to be positing a rule that an Applicant must be limited to claiming only what is present in the working examples (*i.e.*, BQ788 in Example 1 of the instant specification). This is not the law. In fact, there is no requirement that an application have any working examples, even when the invention involves a complex technology. See In re Strahilevitz, 668 F.2d 1229, 212 U.S.P.Q. 561 (C.C.P.A. 1982). Therefore, the fact that Applicants have not identified *all* selective ETB antagonists that can be used in accordance with the claimed methods of the invention is not material to patentability.

The Examiner further alleges that the Applicant is not entitled to the breadth of the claims at issue - namely the use of all selective ETB antagonists in the claimed methods of treating cancer. The Examiner contends that the Applicant is only in possession of one species of ETB antagonist (*i.e.*, BQ788) which is not identified by sequence identity number or defined by structure. Applicants submit that the specification does adequately describe the entire scope of genus of compounds to be used in the claimed methods of the invention. Applicants contend that the specification has provided a description of unifying characteristics that distinguish the members of the genus of compounds to be used in the methods of the invention, *i.e.*, the ability to selectively antagonize ETB.

The function of the "written description" requirement of 35 U.S.C. 112, first paragraph, is to ensure that Applicants had possession of the claimed subject matter, as of the

filing date of application relied on. In re Blaser, 556 F.2d 534, 194 USPQ 122 (CCPA 1977). The inquiry into satisfaction of the written description requirement is factual and depends on the nature of the invention and the amount of knowledge imparted to those of skill in the art by the disclosure. In re Wertheim, 646 F.2d 527, 191 USPQ 90 (CCPA 1976). Satisfaction of the "written description" requirement does not require *in haec verba* antecedence in the originally filed application. In re Lukach, 440 F.2d 1263, 169 USPQ 795 (CCPA 1971). The written description requirement can be satisfied by showing that the disclosed subject matter, when given its 'necessary and only reasonable construction,' inherently (*i.e.*, necessarily) satisfies the limitation in question. Staehelin v. Secher, 24 USPQ2d, 1513, 1520 (Bd. Pat. Int'f. 1992) ("a specification need not describe the exact details for preparing every species within the genus described"). In general, precedent establishes that although the Applicant 'does not have to describe exactly the subject matter claimed, the description must clearly allow persons of skill in the art to recognize that [the Applicant] invented what is claimed.' In re Gosteli, 872 F.2d 1008,1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). "The written description must communicate that which is needed to enable the skilled artisan to make and use the claimed invention." Kennecott Corp. v. Kyocera Int'l, Inc., 835 F.2d 1419, 1421, 5 U.S.P.Q.2d 1194, 1197 (Fed. Cir. 1987), *cert. denied*, 486 U.S. 1008 (1988).

To overcome a prima facie case of unpatentability under 35 U.S.C. § 112, first paragraph, Applicants must show by evidence or argument that the invention as claimed is adequately described to one of ordinary skill in the art. In re Alton 76 F.3d 1168, 1175 (Fed. Cir. 1996). The specification does in fact provide a sufficient disclosure of the claimed genus to allow one of skill in the art to identify other members of the genus to be used in accordance with the claimed methods.

In the present situation, Applicants are not claiming the compounds themselves, but a new use for compounds that are selective antagonists of ETB. Through the use of *in vitro* assays as described in the instant specification, compounds with the desired property (*i.e.*, selective inhibition of ETB activity) can be identified. Applicants have demonstrated various means of identifying a compound to be a *selective* antagonist of ETB, including, but not limited to prevention of downregulation of E-cadherin protein levels (*e.g.*, page 47, line 26 to page 48, line 4 and page 48, lines12-22 of the instant specification); prevention of downregulation of β-catenin protein levels and/or prevention of increased electrophoretic mobility of the β-catenin protein (*e.g.*, page 49, lines 10-14 of the instant specification); prevention of downregulation of $p120^{CTN}$ protein levels and/or prevention of increased electrophoretic mobility of the $p120^{CTN}$ protein (*e.g.*, page 49, lines 16-18 of the instant specification); and prevention of increased caspase 8 activity levels (*e.g.*, page 50, line 18 to page 51, line 3 of the instant specification). One of skill in the art can easily subject candidate compounds to *in vitro* assays to discern genus members from non-genus members. Using this criteria, *any* compound can be determined by one skilled in the art to be either inside or outside of the genus without resorting to undue experimentation.

In view of the foregoing, Applicants request that the Examiner withdraws the rejections under 35 U.S.C. §112, first paragraph.

The Rejections Under 35 U.S.C. § 102 Should Be Withdrawn

Claims 1-4, and 14 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,063,911 to Vournakis ("Vournakis"). The Examiner contends that Vournakis discloses an endothelin antagonist that can be used in a method for treating cancer, particularly melanoma. This rejection is in error and should be withdrawn.

The Examiner has allegedly considered Applicants' previous arguments that amended claims reciting *selective* ETB antagonists are not anticipated by Vournakis and deemed them non-persuasive because the instant specification allegedly does not define selective ETB antagonists. The Applicants contend that contrary to the Examiner's position, the specification clearly provides to one skilled in the art the parameters to identify a selective antagonist of ETB.

Here the claims relate to a method for treating cancer by administering a compound that *selectively* antagonizes ETB. The instant specification provides a number of compounds with the ability to selectively antagonize ETB. Example 1 shows that, unlike a known ETA antagonist (BQ123), a known selective ETB antagonist (BQ788) does indeed down-regulate endothelin dependent E-cadherin expression and act as a selective ETB antagonist. Clearly, the claimed method is enabled by the compounds enumerated in the specification, as well as those known in the art. The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. U.S. v. Telectronics Inc., 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). The specification need not, and preferably should not describe what is already known in the art. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986).

With respect to compounds which have heretofore unappreciated selective ETB antagonistic activity, the specification discloses assays for the identification of such compounds. The specification explicitly states that the compounds that can be used in the methods of the invention are not limited to the specific examples disclosed, and describes assays that can be used to determine the specificity of candidate compounds for use in the

method of the invention. As set out in the specification, appropriate compounds may be identified by their ability to selectively bind to ETB or to modulate the interaction between ETB and its binding partner(s) (*e.g.*, Sections 5.6.1 and 5.6.2 of the instant specification). Compounds can also be identified by their ability to functionally inhibit ETB. For example, Applicants have demonstrated various means of identifying a compound to be a *selective* antagonist of ETB, including, but not limited to prevention of downregulation of E-cadherin protein levels (*e.g.*, page 47, line 26 to page 48, line 4 and page 48, lines12-22 of the instant specification); prevention of downregulation of β-catenin protein levels and/or prevention of increased electrophoretic mobility of the β-catenin protein (*e.g.*, page 49, lines 10-14 of the instant specification); prevention of downregulation of $p120^{CTN}$ protein levels and/or prevention of increased electrophoretic mobility of $p120^{CTN}$ protein (*e.g.*, page 49, lines 16-18 of the instant specification); and prevention of increased caspase 8 activity levels (*e.g.*, page 50, line 18 to page 51, line 3 of the instant specification). One of skill in the art can readily use the assays taught in the specification to determine whether a candidate compound has activity as a selective endothelin B receptor antagonist or not. Therefore, the skilled artisan can obtain from the specification sufficient knowledge of the types of compounds that can be used in the methods of the claimed invention such that the methods are effective in treating cancer.

Someone skilled in the art could use the teachings of the specification to identify selective ETB antagonists without undue experimentation to distinguish those compounds which may be used in accordance with the claimed methods of the invention. Thus, the Examiner's contention that the specification does not define selective antagonists of ETB or does not give direction as to what would characterize a selective ETB antagonist is in error.

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. W.L. Gore Associates v. Garlock, Inc., 721 F.2d 1540, 1554 (Fed.Cir. 1983) cert. denied 469 U.S. 851 (1984); In re Donohue, 766 F.2d 531 (Fed. Cir. 1985). Anticipation under 35 U.S.C. § 102 requires identity of invention. Scripps Clinic & Research Fdn. v. Genentech Inc., 927 F.2d 1565 (Fed. Cir. 1991).

In the present instance, Vournakis does not describe a method of treating cancer comprising administering a *selective* antagonist for the endothelin B receptor. Rather, the compound disclosed in Vournakis, RO61, is a non-specific, non-peptide inhibitor of both endothelin receptors, ETA and ETB (see column 3, lines 44-46 of Vournakis). Since each and every limitation of the claimed invention is not disclosed in the prior art reference, the invention is not anticipated, and the rejection should be withdrawn.

Claims 1-4, and 14 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,382,569 to Cody ("Cody"). The Examiner contends that Cody discloses novel antagonists of endothelin that are receptor antagonists useful in treating cancer. The rejection is in error and should be withdrawn.

Applicants respectfully point out that this rejection is a duplicate of a rejection made in the Office Action mailed February 23, 2001 in paragraph 10 (a copy of which is submitted herewith as Exhibit 1). Applicants responded to this rejection with arguments in the Amendment Under 37 C.F.R. § 1.111 filed August 23, 2001 on pages 7-8 (a copy of which is submitted herewith as Exhibit 2). The Examiner found these arguments to be persuasive and thus withdrew the rejection in the Office Action mailed November 6, 2001 in

paragraph 8 (a copy of which is submitted herewith as Exhibit 3). Applicants believe that no additional arguments are required to obviate this rejection.

In view of the foregoing, the rejections under 35 U.S.C. § 102 should be withdrawn.

CONCLUSION

Applicants respectfully request entry and consideration of the foregoing amendments and remarks. The claims are believed to be free of the art, and patentable. Withdrawal of all the rejections and objections and allowance is earnestly sought.

Respectfully submitted,

by: Jacqueline Benn
Reg No 43,492

Date December 4, 2002

Laura A. Coruzzi 30,742

Laura A. Coruzzi (Reg. No.)

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Enclosure

APPENDIX A
Marked-Up Copy of the Amended Claims
U.S. Patent Application Serial No. 09/305,084
Attorney Docket No. 5914-080-999

4. The method of Claim 1, in which the compound is a mimic of Endothelin-1 that selectively binds to the endothelin B receptor.

APPENDIX B

Pending Claims as of December 4, 2002
U.S. Patent Application Serial No. 09/305,084
Attorney Docket No. 5914-080-999

1. A method for treating a cancer comprising administering a compound that is a selective antagonist to an endothelin B receptor, to a patient in need thereof.

2. The method of Claim 1 in which the cancer is selected from the group consisting of melanoma, prostate cancer, colon cancer, ovarian cancer or mammary cancer.

3. The method of Claim 2 in which the cancer is melanoma.

4. (amended) The method of Claim 1, in which the compound is a mimic of Endothelin-1 that selectively binds to the endothelin B receptor.

5. The method of Claim 1 in which the compound is an antisense molecule that blocks translation of a polypeptide that activates the endothelin B receptor.

14. The method for treating cancer wherein the cancer cells express the endothelin B receptor, comprising administering a compound that is a selective antagonist to the endothelin B receptor to a patient in need of such treatment.

15. A method for treating cancer comprising administering a compound that prevents the downregulation of E-cadherin in the cancer cell to a patient in need of such treatment.

16. (new) A method for treating cancer comprising administering a compound that is a selective antagonist to an endothelin B receptor such that it prevents the downregulation of β-catenin in the cancer cell to a patient in need of such treatment.

17. (new) A method for treating cancer comprising administering a compound that is a selective antagonist to an endothelin B receptor such that it prevents the downregulation of $p120^{CTN}$ in the cancer cell to a patient in need of such treatment.

18. (new) A method for treating cancer comprising administering a compound that is a selective antagonist to an endothelin B receptor such that it prevents the increased activity of caspase 8 in the cancer cell to a patient in need of such treatment.

19. (new) The method of claim 1 wherein the compound that is a selective antagonist to an endothelin B receptor is determined by an *in vitro* assay comprising:

a) contacting a cell expressing endothelin B receptor and E-cadherin with endothelin and the compound; and

b) determining the level of E-cadherin expression,

wherein the level of E-cadherin expression in cells contacted with endothelin in the absence of the compound is decreased compared to the level of E-cadherin expression in cells contacted with endothelin and the compound.

20. (new) A method for treating a cancer, comprising administering to a patient in need thereof a selective endothelin B receptor antagonist compound selected from the group consisting of BQ788, IRL-1038, RES-701-1, PD-142893, and H-3596.

Exhibit 1

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/305,084	05/04/99	SCHNEIDER R	5914-080-999

24

020583
PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK NY 10036-2711

HM12/0223

EXAMINER	
HARRIS, A	
ART UNIT	PAPER NUMBER
1642	08

DATE MAILED: 02/23/01

Amendment due 5/23/01 WT

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

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MAR 14 2001
Pennie & Edmonds
O.K. for filing

PTO-90C (Rev. 2/95)

2 - Mail Copy

Office Action Summary

Application No.	Applicant(s)
09/305,084	Schneider And Jamal
Examiner	**Group Art Unit**
Alana M. Harris, Ph. D.	1642

☒ Responsive to communication(s) filed on *December 13, 2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire ~~3~~ month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-5* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-5* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4 and 7.*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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Sheet 1 of 1

LIST OF REFERENCES CITED BY APPLICANT

(Use several sheets if necessary)

ATTY. DOCKET NO.	APPLICATION NO.
5914-080-999	09/305,084
APPLICANT	
Schneider *et al.*	
FILING DATE	**GROUP**
May 4, 1999	1642

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	EK	5,550,110	8/27/96	Cody et al.			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

OTHER REFERENCES (*Including Author, Title, Date, Pertinent Pages, Etc.*)

	EL	Kikuchi et al., 1996, Biochem. Biophys. Res. Commun., 219:734-739

EXAMINER	DATE CONSIDERED
Ann Harris	February 20, 2001

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

ATTY. DOCKET NO.	APPLICATION NO.
5914-080-999	09/305,084
APPLICANT: Schneider et al.	
FILING DATE: 05/04/99	GROUP: 1640 ~~1642~~

LIST OF REFERENCES CITED BY APPLICANT

(Use several sheets if necessary)

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
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	AQ	5,464,853	11/07/95	Chan et al.			
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	AT	A1 0 496 452	07/29/92	EP				
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	AV	A1 0 569 193	11/10/93	EP				
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	AY	WO 92/06180	04/16/92	PCT				
	AZ	WO 92/20316	11/26/92	PCT				
	BA	WO 92/22635	12/23/92	PCT				

amh	BC	WO 93/14188	07/22/93	PCT	—	—		
	BD	WO 93/20221	10/14/93	PCT	—	—		
	BE	WO 94/27979	12/08/94	PCT	—	—		

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	DT	Shimoyama et al., 1992, Cancer Res., 52:5770-5774
	DU	Songyang, Z. et al., 1993, Cell, 72:767-778

	DW	Tanaka *et al.*, 1994, *Mol. Pharmacol.*, 45:724-730
	DX	Tang, et al., 1994, *J. Cell. Sci.*, 107:983-92
	DY	Thornberry, *et al.*, 1998, *Science*, 261:1312-8
	DZ	Tohma, et al., 1992, Cancer Research, 52: 1981-1987
	EA	Tomita et al., 1989, N. Engl. J. Med. 321:1127
	EB	Umbas, et al., Cancer Research, 1992, 52:5104-5109
	EC	Urade *et al.*,1992, *FEBS Lett.*, 311:12-16
	ED	Valyi-Nagy et al., 1993, *Lab Invest.*, 69:152-9
	EE	Vanhoutte et al., 1986, Annual Rev. Physiol., 48: 307-320
	EF	Vermeulen, et al., 1996, *Pathol. Res. Pract.*, 192: 694-707
	EG	von Geldern et al., 1991, Peptide Res., 4: 32-35
	EH	Wu and Wu, 1987, J. Biol. Chem., 262:4429-4432
	EI	Yamanishi et al., 1992, Cancer Res., 52:5024-5029
	EJ	Zijlstra et al., 1989, Nature, 342:435-438

EXAMINER- [signature] DATE CONSIDERED 2/12/2001

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Includ copy f this form with next communication to applicant.

FORM PTO 948 (REV. 01-97) U.S. DEPARTMENT OF COMMERCE-Patent and Trademark Office Application No. 9/305,084

NOTICE OF DRAFTPERSON'S PATENT DRAWING REVIEW

The drawing filied (insert date) 5.4.99 are:

A. _____ not objected to by the Draftperson under 37 CFR 1.84 or 1.152.

B. / objected to by the Draftperson under 37 CFR 1.84 or 1.152 as indicated below. The Examiner will require submission of new, corrected drawings whe necessary. Corrected drawings must be submitted according to the instructions on the back of this notice.

1. DRAWINGS. 37 CFR 1.84(a): Acceptable categories of drawings:
Black ink. Color.
_____ Color drawing are not acceptable until petition is granted.
Fig.(s)_____
_____ Pencil and non black ink is not permitted. Fig(s)_____

2. PHOTOGRAPHS. 37 CFR 1.84(b)
_____ Photographs are not acceptable until petition is granted.
_____ 3 full-tone sets are required. Fig(s)_____
_____ Photographs not properly mounted (must brystol board or photographic double-weight paper). Fig(s)_____
/ Poor quailty (half-tone). Fig(s) 4

3. TYPE OF PAPER. 37 CFR 1.84(e)
_____ Paper not flexible, strong, white and durable.
Fig.(s)_____
_____ Erasures, alterations, overwritings, interlineations, folds, copy machine marks not acceptable. (too thin)
_____ Mylar, vellum paper is not acceptable (too thin).
Fig(s)_____

4. SIZE OF PAPER. 37 CFR 1.84(F): Acceptable sizes:
_____ 21.0 cm by 29.7 cm (DIN size A4)
_____ 21.6 cm by 27.9 cm (8 1/2 x 11 inches)
_____ All drawings sheets not the same size.
Sheet(s)_____

5. MARGINS. 37 CFR 18.4(g): Acceptable margins:
Top 2.5 cm Left 2.5 cm Right 1.5 cm Bottom 1.0 cm
SIZE: A4 Size

7. SECTIONAL VIEWS. 37 CFR 1.84(h)(3)
_____ Hatching not indicated for sectional portions of an object.
Fig.(s)_____
_____ Sectional designation should be noted with Arabic or Roman numbers. Fig.(s)_____

8. ARRANGEMENT OF VIEWS. 37 CFR 1.84(i)
_____ Words do not appear on a horizontal, left-to-right fashion when page is either upright or turned, so that the top becomes the right side, except for graphs. Fig.(s)_____
_____ Views not on the same plane on drawing sheet. Fig.(s)_____

9. SCALE. 37 CFR 1.84(k)
_____ Scale not large enough to show mechanism with crowding when drawing is reduced in size to two-thirds in reproduction.
Fig.(s)_____

10. CHARACTER OF LINES, NUMBERS, & LETTERS. 37 CFR 1.84(l)
_____ Lines, numbers & letters not uniformly thick and well defined, clean, durable and black (poor line quality).
Fig.(s)_____

11. SHADING. 37 CFR 1.84(m)
_____ Solid black areas pale. Fig.(s)_____
_____ Solid black shading not permitted. Fig.(s)_____
_____ Shade lines, pale, rough and blurred. Fig.(s)

12. NUMBERS, LETTERS, & REFERENCE CHARACTERS. 37 CFR 1.48(p)
_____ Numbers and reference characters not plain and legible.
Fig.(s)_____

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claim 1-5) in Paper No.6 (filed December 13, 2000) is acknowledged. The traversal is on the grounds that it would not be a serious burden on the Examiner to search Groups I and II at the same time and in the belief that the Examiner incorrectly classified Group II. This is unpersuasive.

The argument that a search encompassing the two Groups is not found persuasive for the reasons set forth in the restriction requirement (Paper No. 5, mailed November 17, 2000). The Examiner does concur with Applicants that the subclass of Group II was incorrect, however this does not warrant removal of the restriction requirement. The correct subclass is 7.6. The method clearly involves two different molecules, an antisense molecule and a ribozyme. As to the question of burden of search, the claims of Groups I and II are classified differently, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is adhered to.

The requirement is therefore made FINAL.

However, the policies set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86 will be followed. Method claims limited to the scope of the allowable product claims will be rejoined and examined at the time the product claims are indicated as being allowable.

2. Claims 1-5 are pending.

Claims 6-13 have been canceled.

Claims 1-6 examined on the merits.

Drawings

3. The drawings are objected to because of reasons cited on attached form, PTO-948 completed by draftsman. Correction is required.

Specification

4. The disclosure is objected to because the brief description of the drawings section, specifically Figure 4 on page 19, lines 23-27 of the specification does not contain a separate description of figures 4a-4j. A figure caption for each panel within a figure must be cited within the brief description of the drawings section.

Claim Objections

5. Claim 5 is objected to because the claim contains the recitation " or ribozyme" and Applicants have elected the method of Group I in which the compound is an antisense molecule. The recitation "or ribozyme" must be deleted from the claim.

Claim Rejections - 35 U.S.C. § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 1 is broadly drawn to "A method for treating a cancer, comprising administering a compound ... to a subject in need of such treatment." These claims read on any and all compounds capable of treating any and all cancers. While the specification teaches the administration of compounds, BQ7°8 and BQ123 to melanocytes and melanoma cell lines, the specification does not teach the administration of any compound to any and all cancers other than melanoma . Many compounds could be administered to a cancer patient in hopes of treatment,

however Applicants have provided just one example of melanoma treatment, exemplified in Example 1 found on pages 47 and 48. Thus the specification is only enabled for the method of treating a melonoma cancer comprising administering BQ788 and BQ123, antagonists of endothelin B receptor. It would require undue experimentation of one skilled in the art to make and use all compounds considered anti-cancer agents that would be possibly effective in the treatment of a cancer.

Likewise, it is well known in the art of cancer treatment that tumors of differing cell types respond differently to a given therapeutic approach, and that a treatment modality that is effective against of a tumor of one given cell type would not necessarily be expected to be effective against tumors of differing histological origin. Cancers of all cell types are not expected, by those of skill in the art, to respond in a similar fashion to the administration of a given class of molecules.

Additionally, the reference by Johnson and Goldin (Cancer Treatment Reviews 2:1-31, 1975) cites that neoplasms of different cell origins respond very differently to a given anti-tumor agent. Table 2 on page 5 is a comparison of the activity spectrum of anti-tumor agents in a variety of human tumors. Note, for example, that methotrexate is effective against acute lymphocytic leukemia, breast, lung, head and neck, cervical and testicular cancers and trophoblastic tumors (and ineffective against gastrointestinal carcinoma, chronic myelogenous leukemia, malignant melanoma and sarcoma), while mitomycin C is effective against gastrointestinal carcinoma (and ineffective against acute lymphocytic leukemia, breast, lung, head and neck, cervical and testicular cancers, trophoblastic tumors, chronic myelogenous leukemia,

malignant melanoma and sarcoma) and hydroxyurea is effective against chronic myelogenous leukemia, malignant melanoma and sarcoma (and ineffective against acute lymphocytic leukemia, breast, lung, head and neck, cervical and testicular cancers, trophoblastic tumors and gastrointestinal carcinoma). Thus, as supported by the Johnson and Goldin reference, one of skill in the art would not expect a suggested anti-tumor agent, such as an neurotoxin, to be effective against neoplasms of differing histological origin. Thus, one of skill in the art could not practice the broadly claimed method, of treating cancers of all cell types, with a reasonable expectation of success.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "the compound is a mimic" in claim 4 is vague and indefinite. It is not clear in what fashion should the compound resemble or imitate endothelin-1? Should it mock endothelin-1 in structure, activity or binding affinity for the receptor? The metes and bounds cannot be determined.

b. Claim 5 is vague and indefinite in the recitation "molecule". What is the molecule that is claimed to activated ETB? The metes and bounds of the claim cannot be determined. A "molecule" can be anything, such as a peptide, an organic molecule, an inorganic molecule, a DNA fragment, a plastic, a carbohydrate, etc. Applicant's attention is directed to Ex Parte Tanksley (26 USPQ2d 1384) wherein the Board noted that under 35 U.S.C. 112, second paragraph, the claims must be so definite as to allow the comparison with the available art and must also make it possible for the public to determine from the claim what it encompasses. How would one know if the patented claim was being infringed?

c. Claim 5 is vague and indefinite in the recitation "...a molecule that activates ETB." In what manner is this molecule to activate ETB? Hence, the metes and bounds of the claim cannot be determined.

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10. Claims 1 and 4 rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,382,569 (January 17, 1995)/ Reference AP on IDS. U.S. Patent #5,382,569 discloses novel antagonists of endothelin that are antagonists to an ETB which are useful in treating cancer. These antagonists also mimic endothelin-1, see the abstract.

11. Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by Okazawa et al. (Journal of Biological Chemistry 273(20):12584-12592, May 15, 1998)/ Reference DC on IDS. Okazawa discloses a method for treating melanoma cancer comprising administering BQ788, see Figure 2d. This compound is a mimic of endothelin-1, see Figure 1 caption and page 12588, column 1, sentence 2.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703)306-5880. The examiner can normally be reached on Monday through Friday from 6:30 am to 3:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703)308-4310. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703)308-0196.

Sheela J. Huff
SHEELA HUFF
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
February 20, 2001

Notice of References Cited

Application N .	Applicant(s)		
09/305,084	Schneider And Jamal		
Examiner		Group Art Unit	Page 1 of 1
Alana M. Harris, Ph. D.		1642	

U.S. PATENT DOCUMENTS

		DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS
	A					
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUBCLASS
	N						
	O						
	P						
	Q						
	R						
	S						
	T						

NON-PATENT DOCUMENTS

		DOCUMENT (Including Author, Title, Source, and Pertinent Pages)	DATE
	U	Johnson and Goldin. The clinical impact of screening and other experimental tumor studies. Cancer Treatment Reviews 2:1-31.	1975
	V		
	W		
	X		

Exhibit 2

EXPRESS MAIL NO.: EL 168 272 557 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: SCHNEIDER AND JAMAL

Application No.: 09/305,084 Group Art Unit: 1642

Filed: May 4, 1999 Examiner: A. Harris

For: **CANCER TREATMENT WITH ENDOTHELIN RECEPTOR ANTAGONISTS** Attorney Docket No.: 5914-080-999

AMENDMENT UNDER 37 C.F.R. § 1.111

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the outstanding Office Action mailed February 23, 2001, please enter the following amendments and consider the remarks made below in connection with the above-identified application. Also submitted concurrently are: (a) a Petition to Extend Time accompanied by the required fee; (b) a marked-up version of the paragraph amended herein as Appendix A; (c) a marked-up version of the claims amended herein as Appendix B; (d) a clean copy of the claims as pending in the present application after entry of the present amendment as Appendix C; (e) replacement informal Figures 1-4 as Appendix D; (f) Egidy et al., 2000, *Lab Invest* 80:1681-9, submitted herewith as Exhibit 1; and (g) Alanen et al., 2000, *Histopatholog* 36:161, submitted herewith as Exhibit 2.

IN THE SPECIFICATION

Please amend the specification to read as follows:

On page 19, please replace the third full paragraph with the following:

Figure 4: ET-1 alters the subcellular localization of E-cadherin and β-catenin. Cells were incubated either with or without 10nM ET-1 for 96 hours then fixed and stained with anti- E-cadherin or anti-β-catenin antibodies followed by anti-mouse-IgG-Cy3 antibodies. E-cadherin localization is shown for melanocytes either (A) without or (B) with ET-1 incubation and in melanoma cells either (C) without or (D) with ET-1 incubation. β-catenin localization is shown for melanoma cells either (E) without or (F) with ET-1 incubation and in melanocytes either (G) without or (H) with ET-1 incubation. Melanocyte cell morphology is shown by bright field micrographs of cells either (I) without or (J) with ET-1 incubation. Incubation of melanocytes and melanoma cells with secondary antibody alone revealed no background staining.

IN THE CLAIMS

Please amend claims 1, 4, and 5 to read as follows:

1. A method for treating a cancer, comprising administering a compound that is a selective antagonist to an endothelin B receptor.

4. The method of Claim 1, in which the compound is a mimic of Endothelin-1 that binds to the endothelin B receptor.

5. The method of Claim 1 in which the compound is an antisense molecule that blocks translation of a polypeptide that activates the endothelin B receptor.

Please add new Claims 14 and 15.

14. (new) A method for treating cancer, wherein the cancer cells selectively express the endothelin B receptor, comprising administering a compound that is an antagonist to an endothelin B receptor to a subject in need of such treatment.

15. (new) A method for treating cancer, comprising administering a compound that prevents the downregulation of E-cadherin in the cancer cell to a subject in need of such treatment.

REMARKS

Claims 1-5 are presently pending. Claims 1, 4, and 5 have been amended to more particularly point out and distinctly claim the invention; to place the claims in condition for allowance. The specification has been amended to include separate descriptions of Figures 4A-J in the Brief Description of the Drawings section. No new matter has been added (*see e.g.*, the instant specification on page 51, line 31 to page 52, line 19). New Claims 14 and 15 are fully supported by the instant specification. In particular, support can be found, e.g., on page 15, lines 22-24 and on page 48, lines 8-18. Support for the claim amendments may be found in the instant specification, thus, no new matter has been introduced. In particular, support for the amendment to Claim 1 can be found, *e.g.*, on page 15, lines 15-21; page 19, line 30 to page 20, line 18; and page 55, lines 3-7. Support for the amendment to Claim 4 can be found, *e.g.*, on page 16, lines 1-6; page 22, lines 19-21; page 24, lines 8-11; and page 25, line 22-25. Support for the amendment to Claim 5 can be found, *e.g.* on page 17, lines 3-7. Entry of the foregoing amendments are respectfully requested.

A marked up version of the replacement paragraph and amended claim showing the amendments is attached hereto as Appendices A and B, respectively. Matter that has been deleted is indicated by brackets and matter that has been added is indicated by

underlining. A copy of the claims as pending after entry of the foregoing amendment is attached as Appendix C.

The Drawings

The drawings have been objected to and require correction. Submitted herewith as Appendix D are replacement informal Figures 1-4. Applicants will submit formal drawings should subject matter be found allowable.

The Rejections Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

Claims 1-5 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement commensurate with the scope of the claimed invention. The Examiner contends that the specification only teaches administration of endothelin receptor inhibitors to melanoma cells, as such, administration of any compound to any and all cancers other than melanomas is not enabled. This rejection is in error and should be withdrawn.

The specification teaches methods designed to target ET-1 mediated initiation of cancer (*see e.g.*, the instant specification on page 19, line 30 to page 20, line 2). The specification provides that the invention relates to the treatment and prevention of cancers including, but not limited to, melanoma, prostate cancer, colon cancer, ovarian cancer, and mammary cancers using compounds that antagonize the endothelin B receptor or result in the prevention of downregulation of E-cadherin (*see e.g.*, page 15 of the instant specification). The instant application has enabled the treatment of each of these cancers and, has provided evidence of such enablement through the data supplied in the Working Examples demonstrating the successful treatment of melanoma (see, the instant specification at pages 47-52). According to applicable case law, an inventor is not required to disclose "a test of *every* species encompassed by their claims" even in an unpredictable art. *In re Angstadt*, 190

U.S.P.Q. 214, 218 (C.C.P.A. 1976) (emphasis in original). Accordingly, the scope of the claims should not be limited to one species (*i.e.*, melanoma) when the methods of the present invention are applicable to a genus of cancers.

Cancers in the genus could be identified by one of ordinary skill in the art. A literature search of the NCBI PubMed database (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed) quickly revealed a number of post-filing publications describing cancers other than melanoma that could be treated by the addition of endothelin B receptor antagonists. For example, glioblastoma cancer cells were found to undergo apoptosis upon the addition of an endothelin receptor antagonist (Egidy et al., 2000, *Lab Invest* 80:1681-9; submitted herewith as Exhibit 1). Although the antagonist used was capable of inhibiting both types of endothelin receptors, the cancer cells were shown to express endothelin B receptor and ET-1 was mainly acting via that pathway. Additionally, breast cancer cells were shown to express elevated levels of endothelin B receptor as compared to their normal counterparts (Alanen et al., 2000, *Histopatholog* 36:161; submitted herewith as Exhibit 2). Even though cancers of differing cell types have been reported to respond differently to a given therapeutic approach, all cancers with a common basis (*e.g.*, ET-1 signaling through the endothelin B receptor) should all be improved by targeting that unifying characteristic (*e.g.*, decreased or inhibited signaling through the endothelin B receptor).

In view of the foregoing, the rejections under 35 U.S.C. § 112, first paragraph are obviated and should be withdrawn.

The Rejections Under 35 U.S.C. § 112, Second Paragraph Should Be Withdrawn

Claims 4 and 5 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is in error and should be withdrawn.

The Examiner contends that the recitation of "the compound is a mimic" in claim 4 is vague and indefinite because it is not clear what aspect of endothelin-1 is to be mimicked. Applicants have amended claim 4 to recite the aspect of endothelin-1 that is of relevance – namely its ability to bind to the endothelin B receptor (see, *e.g.*, page 25, lines 22-25 of the instant specification).

The Examiner contends that the recitation of "molecule" in claim 5 is vague and indefinite because it is not clear what type of molecule that activates the endothelin B receptor is encompassed by the claim. Applicants have amended claim 5 to clarify that the type of molecule is a polypeptide (*i.e.*, the only type of molecule that is translated).

The Examiner contends that the recitation of "a molecule that activates endothelin B receptor" is vague and indefinite because the manner in which receptor activation occurs is unclear. Applicants assert that the *manner* of activation is not important - only that the receptor becomes active. Someone of skill in the art could use common molecular biological techniques to devise an *in vitro* assay to determine if the endothelin receptor has been activated without undue experimentation. The instant specification clearly discloses a number of consequences of receptor activation that could be used as a readout in such an assay including downregulation of E-cadherin, $p120^{CTN}$, and β-catenin as well as activation of caspase-8 (see, *e.g.*, page 15, lines 22-25 of the instant specification).

In view of the foregoing, the rejections under 35 U.S.C. § 112, second paragraph are obviated and should be withdrawn.

The Rejections Under 35 U.S.C. § 102 Should Be Withdrawn

Claims 1 and 4 are rejected under 35 U.S.C § 102(e) as being anticipated by U.S. Patent No. 5,382,569 (the "'569 patent"). The Examiner contends that the '569 patent discloses novel antagonists of endothelin that are receptor antagonists useful in treating cancer. This rejection is in error and should be withdrawn.

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. W.L. Gore Associates v. Garlock, Inc., 721 F.2d 1540, 1554 (Fed.Cir. 1983) cert. denied 469 U.S. 851 (1984); In re Donohue, 766 F.2d 531 (Fed. Cir. 1985). Anticipation under 35 U.S.C. § 102 requires identity of invention. Scripps Clinic & Research Fdn. v. Genentech Inc., 927 F.2d 1565 (Fed. Cir. 1991).

In the present instance, the '569 patent does not describe a method of treating cancer comprising administering a selective antagonist for the endothelin B receptor; therefore, the invention is not anticipated.

The '569 patent describes that elevated levels of endothelin have been postulated to be involved in a number of diseases. The '569 patent provides a list of antagonists of endothelin which may be useful in treating disorders related to elevated levels of endothelin. Also disclosed are a laundry list of proposed disorders which may be candidates for treatment with the endothelin (ET-1) antagonists. Candidate disorders were selected due to reports in the literature of elevated levels of circulating ET-1 in the plasma of

individuals suffering from such disorders. Table I in column 5 of the '569 patent lists the diverse array of disorders compiled in this manner.

There is no identification or recognition in the '569 patent that a cancer can be treated by the administration of a compound that acts to selectively antagonize the endothelin B receptor. Further, there is no identification or recognition in the '569 patent that a cancer wherein the cancer cells selectively express the endothelin B receptor, can be treated by the administration of a compound that is an antagonist of the endothelin B receptor (new Claim 14). Furthermore, there is no identification or recognition in the '569 patent that a cancer can be treated by the administration of a compound that prevents the downregulation of E-cadherin (new Claim 15).

Thus, in view of the foregoing, as anticipation requires identity of the claimed invention, the '569 patent cannot anticipate the invention as claimed. Therefore, the rejection under § 102(e) in view of the '569 patent is in error and should be withdrawn.

In the present instance, Okazawa does not describe a method of treating cancer comprising administering a selective antagonist for the endothelin B receptor; therefore, the invention is not anticipated.

Claims 1-4 are rejected under 35 U.S.C § 102(a) as being anticipated by Okazawa et al., 1998 *J. Biol. Chem.* 273:12584-92 ("Okazawa"). The Examiner erroneously interprets Okazawa as disclosing a method of treating melanoma cancer comprising administering BQ788. This rejection is in error and should be withdrawn.

Okazawa reports experiments done to characterize the effects of ET-1, an antagonist of ET receptors, on a culture of cell cycle synchronized A375 melanoma cells. Such effects included the ability of ET-1 to induce cell death or apoptosis of the melanoma cells. Okazawa reports that an antagonist of ET receptors, such as BQ788, was able to

prevent ET-1 induced apoptosis of melanoma cells. BQ788 was used to rescue cell death of melanoma cells induced by ET-1. Thus, the Examiner is incorrect in his allegation that Okazawa teaches the use of BQ788 in the treatment of melanoma. Okazawa, in fact, teaches just the opposite. According to the teaching of Okazawa, one would administer an agonist of an ET receptor to induce cell death of a melanoma cell and administer an antagonist of an ET receptor to rescue the melanoma cell from cell death. Thus, there is no identification or recognition in Okazawa that a cancer can be treated by administering a compound that acts to selectively antagonize the endothelin B receptor. Further, there is no identification or recognition in Okazawa that a cancer that selectively expresses the endothelin B receptor, can be treated by the administration of a compound that is an antagonist of the endothelin B receptor (new Claim 14). Furthermore, there is no identification or recognition in Okazawa that a cancer can be treated by the administration of a compound that prevents the downregulation of E-cadherin (new Claim 15).

Thus, in view of the foregoing, as anticipation requires identity of the claimed invention, Okazawa cannot anticipate the invention as claimed. Therefore, the rejection under § 102(a) in view of Okazawa is in error and should be withdrawn.

In view of the foregoing, the rejections under 35 U.S.C. § 102 should be withdrawn.

MISCELLANEOUS

Claim 5 was objected to because of the inclusion of the term "or ribozyme". The Examiner contends that ribozymes are the subject matter of Group II rather than elected Group I in the Restriction Requirement mailed November 17, 2000 in connection with the instant application. Consequently, Applicants have deleted the term objected to from claim 5

without prejudice, but reserve the right to prosecute the deleted subject matter in future continuation, continuation-in-part, or divisional applications.

CONCLUSION

Applicants respectfully request entry and consideration of the foregoing amendments and remarks. The claims are believed to be free of the art, and patentable. Withdrawal of all the rejections and objections and allowance is earnestly sought.

Respectfully submitted,

by: Jacqueline Bern
Reg No. 43,492

Date August 23, 2001

Laura A. Coruzzi 30,742

Laura A. Coruzzi (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosure

Exhibit 3

EPARTMENT OF COMMERCE
ent and Trademark Offic
ER OF PATENTS AND TRADEMARKS
C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/305,084	05/04/99	SCHNEIDER R	5914-080-999

EXAMINER	
HARRIS, A	
ART UNIT	PAPER NUMBER
1642	11

020582
PENNIE & EDMONDS LLP
1667 K STREET NW
SUITE 1000
WASHINGTON DC 20006

HM22/1106

DATE MAILED: 11/06/01

Amendment
2-06-02 ACF

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

REFERRED TO CRG/Weir
RECEIVED PEDC
NOV 12 2001
O.K. for filing

2

2 - Mail Copy

Office Action Summary	Application N .	Applicant(s)	
	09/305,084	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on th cover sheet with th correspondence address --

eriod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2001* .

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 1-5, 14 and 15 are pending.

Claims 14 and 15 have been added.

Claims 1-5, 14 and 15 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

3. The drawings are objected to because of reasons cited on attached form, PTO-948 completed by draftsman. Correction is required.

Withdrawn Objections

Specification

4. The disclosure is no longer objected to because the brief description of the drawings section contains a separate description of figures 4a-4j.

Claim Objections

5. Claim 5 is no longer objected to because the claim does not contain the recitation " or ribozyme".

Withdrawn Rejections

Claim Rejections - 35 U.S.C. § 112

6. The rejection of claims 1-5 and 14 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is withdrawn in view of Applicants arguments.

7. The rejection of claims 4 and 5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's amendments and arguments.

Claim Rejections - 35 U.S.C. § 102

8. The rejection of claims 1, 4 and newly added claim 14 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,382,569 (January 17, 1995)/ Reference AP on IDS is withdrawn in view of Applicants' arguments.

9. The rejection of claims 1-4 under 35 U.S.C. 102(a) as being anticipated by Okazawa et al. (Journal of Biological Chemistry 273(20):12584-12592, May 15, 1998)/ Reference DC on IDS is withdrawn in light of Applicants' arguments.

New Grounds of Rejection

Claim Rejections - 35 U.S.C. § 112

10. Claims 1-5, 14 and 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "compound" in claims 1, 4, 5, 14 and 15 is vague and indefinite. The metes and bounds of the claim cannot be determined. A "compound" can be anything, such as a peptide, an organic molecule, an inorganic molecule, a DNA fragment, a plastic, a carbohydrate, etc. Applicant's attention is directed to Ex Parte Tanksley (26 USPQ2d 1384) wherein the Board noted that under 35 U.S.C. 112, second paragraph, the claims must be so definite as to allow the comparison with the available art and must also make it possible for the public to determine from the claim what it encompasses. How would one know if the patented claimed was being infringed?

Claim Rejections - 35 U.S.C. § 102

11. Claim 14 is rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,063,911 (filed December 22, 1998). U.S. Patent #6,063,911 discloses an endothelin antagonist in column 3, lines 19-44 that can be used in a method for treating cancer. The disclosed endothelin B receptor is a non-peptide-based pyrimidyl sulfonamide compound. The said compound is 5-Isopropyl-pyridine-2-sulfonic acid [6-(2-hydroxy-ethoxy)-5-(2-methoxy-phenoxy),-2[2-(1H-tetrazol-5-yl)-pyridin-4-yl]-pyrimidin-4-yl]amide sodium salt (1:2), also termed Ro61. This antagonist, alone or in combination with other antitimor agents can be administered to patients to inhibit the growth and/or metastasis of tumor or other neoplastic cells (see bridging paragraph of columns 5 and 6; lines 4-16 of column 6; and Example 13 of columns 31 and 32).

Conclusion

12. Claims 1-5 and 15 are free of the art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703)306-5880. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703)308-4310. Any inquiry of a general nature or relating to the status of this

application or proceeding should be directed to the Group receptionist whose telephone number is

(703)308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
November 5, 2001

Sheela J. Huff
SHEELA HUFF
PRIMARY EXAMINER

Notice of Referenc s Cited

Application N.	Applicant(s)		
09/305,084	Schneider et al.		
Examiner	Group Art Unit	Page 1 of 1	
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U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS
	A	6,063,911	5/16/2000	Vournakis et al.	—	—
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
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FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUBCLASS
	N						
	O						
	P						
	Q						
	R						
	S						
	T						

NON-PATENT DOCUMENTS

*		DOCUMENT (Including Author, Title, Source, and Pertinent Pages)	DATE
	U		
	V		
	W		
	X		

* A copy of this reference is not being funished with this Office action.
(See Manual of Patent Examining Procedure, Section 707.05(a).)